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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,107	10/30/2001	Grant L. Schoenhard	13726US01	8970

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/000,107	SCHOENHARD, GRANT L.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52 and 54-63* is/are pending in the application.

4a) Of the above claim(s) *1-47 and 56-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-52, 54-55 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2005 has been entered.

Amendment Entry

2. The amendment filed September 29, 2005 has been entered. The examiner acknowledges the changes in Figure 1. Claims 48 and 51 have been amended. Claim 53 has been cancelled. Claim 63 has been newly added. Claims 1-47 and 54-62 are withdrawn. Claims 48-52, 54-55 and 63 are under consideration in this office action.

Response to Arguments

3. Applicant's arguments filed September 29, 2005 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The rejection of claims 48-52, 54-55 and 63 under 35 U.S.C. 103(a) as being unpatentable over Minoia et al., (US Patent 5,811,451) is maintained for the reasons already of record. The rejection was on the grounds that it was prima facie obvious to combine the opioid inhibitor of an ABC drug transporter; and an anti-microbial agent as taught by Minoia et al., into a composition since no more than routine skill would have been required to make said combination when the art already teaches the usefulness of the combined components.

Applicants' assert that there is no motivation or suggestion in the art to modify the references in the manner suggested by the office action. However, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, no more than routine skill would have been required to use the claimed opioid inhibitor of an ABC drug transporter; and an anti-microbial agent when they have been taught as useful together in an old process to achieve the expected and beneficial results found when using the separate compounds in a single composition.

Applicants' urge that Minoia et al., only briefly describes the use of antibiotics and does not use the sub-therapeutic amount. However, differences in concentration or

amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Moreover, no more than routine skill is involved in adjusting the amount of a component within the claimed composition. Furthermore, because no specific amounts are claimed, nothing in Minoia et al., teaches away from the use of sub-therapeutic amounts. Therefore the rejection is maintained since applicants' arguments are not found persuasive.

5. The rejection of claims 48-52, 55 and 63under 35 U.S.C. 103(a) as being unpatentable over Bernstein (US Patent 4,466,968) is maintained for reasons already of record. The rejection was on the grounds that no more than routine skill would have been required to combine the claimed opioid inhibitor of an ABC drug transporter; and the anti-microbial agent into a composition when each component has already been taught as useful together in an old process in order to achieve the expected and beneficial results found when using the separate compounds in a single composition.

Thus in response to applicants' argument that there is no suggestion to combine the references, the examiner asserts that it was prima facie obvious to combine the opioid inhibitor of an ABC drug transporter; and the anti-microbial agent taught by Bernstein since each component is already well known in the art. No more than routine skill would have been required to form the claimed composition since each component

is already well known in the art to be used for the very same purpose; moreover, the idea of combining them flows logically from their having been taught in the prior art as useable together.

Applicants' urge that Bernstein by referring to high dose oral antibiotic therapy is teaching away from the use of a sub-therapeutic amount of an antimicrobial agent. It is the examiner's position that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). The invention was directed to an epoxy impregnated fiber-reinforced printed circuit material. The applied prior art reference taught a printed circuit material similar to that of the claims but impregnated with polyester-imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have "relatively acceptable dimensional stability" and "some degree of flexibility," but are inferior to circuit boards impregnated with polyester-imide resins. The court upheld the rejection concluding that applicant's argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since "Gurley asserted no discovery beyond what was known in the art." 27 F.3d at 554, 31 USPQ2d at 1132. Here, applicants' instant claims have not asserted any discovery beyond what was known in the art. Therefore contrary to applicants' argument, the prior art does not teach away from the

instant claims. Furthermore, Bernstein is referring to treating patients having symptoms caused by high dose oral antibiotic therapy. Bernstein is not teaching administering high doses of oral antibiotic therapy with naltrexone or naloxone. Finally, applicants' have failed to define sub-therapeutic amounts, and differences in amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such amount is critical. Here there is no such evidence. Therefore the rejection is maintained since there would have been a reasonable expectation of success since Bernstein already teaches the combined use of an opioid inhibitor and an anti-microbial.

New Grounds of Rejection

Specification

6. The disclosure is objected to because of the following informalities: The specification, particularly at page 6, refers to opioids which do not correspond to the structure shown. There should not be a double bond between C7 and C8 for nalmefene, naltrexone, naltrexol or naloxone. The lengthy specification has not been checked to the extent necessary to determine the presence of all minor errors with respect to the structure. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 49 is drawn to a composition comprising an opioid inhibitor of an ATP-binding cassette (ABC) drug transporter and a sub-therapeutic amount of an anti-microbe agent wherein the ABC drug transporter is a homologue of human PGP1a. The specification at paragraph [00030] states that the term refers to ABC transporters that share at least 80% amino acid sequence identity to an ABC module of human P-glycoprotein 1a (PGP1a). However, there is no evidence of record of a relationship between the structure of the instantly claimed homologue with that of the prior art that would provide any reliable information about the structure of the missing and unidentified portions of the PGP1a homologue. The specification lacks any description of a structure or relevant identifying characteristics of a representative number of

polypeptide homologues sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

The instant specification fails to describe which amino acids can or cannot be added, substituted, or deleted. Similarly the instant specification fails to disclose regions within the sequences where insertions or substitutions can or cannot be tolerated and still achieve a functional PGP1a homologue. One of skill in the art would be reduced to merely altering amino acids which would lead to unpredictable results regarding the polypeptide homologue. Thus, the instant specification fails to provide an adequate description of the identify of a polypeptide that shares at least 80% amino acid sequence identity to an ABC module of human PGP1a. There is no disclosure of any microbe expressing homologues of human PGP1a. Rather the instant specification and examples teach only mammalian cell lines expressing human P-glycoprotein (PGP), see examples 1-4 of the instant specification. Moreover, there are no representative examples of the claimed homologues.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). There is no disclosure of the structure of a sequence with 80% identity to PGP1a. Thus, the skilled artisan cannot envision the detailed structure of the encompassed molecules since the

specification has not defined what the 20% variability can be. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Thus, the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

It is apparent that Applicants' were not in possession of additional polypeptides or homologues, at the time of filing the instant application. Thus, a skilled artisan cannot envision the detailed structure of a homologue; thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Again, the amino acid sequence and corresponding polypeptide itself is required. Currently the generic recitation is insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claim and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention. In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of the claimed method of enhancing the anti-microbial activity of an

anti-microbial agent against a microbe wherein the ABC drug transporter is a homologue of human PGP1a. Therefore the full breadth of the claim fails to meet the written description provision of 35 USC 112, first paragraph.

8. Claims 48-52, 54-55 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The phrase "sub-therapeutic amount" in the claim is a relative phrase which renders the claim indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither the specification nor the claims define the precise amount or even provide a range of amounts such that one of ordinary skill in the art would known what amounts would be considered a sub-therapeutic amount of anti-microbial agent. Thus the metes and bounds of the phrase are unclear. Therefore clarification is required to overcome the rejection.

a) Claim 49 is indefinite. The acronym PGP1a must be spelled out when used for the first time in a chain of claims.

b) Claim 50 recites the limitation "the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, the tetracyclines, the pristamycins, the aminoglysides, the rifamycins, the quinolones, and the sulfonamides" within the claim. There is insufficient antecedent basis for these limitations in the claim.

c) Claim 55 recites the limitation "the pharamachore" within the claim. There is insufficient antecedent basis for this limitation in the claim.

d) Claim 63 recites that phrase "wherein the anti-microbial agent is adapted to inhibit a microbe...". It is unclear how the agent is adapted or what adaptations have taken place. It is unclear if the same or different adaptations need to occur based upon the selected microbe. Therefore the claim is unclear and indefinite. Furthermore, the phrase is a relative phrase which renders the claim indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither the specification nor the claims define the adaptations necessary to inhibit the selected microbe such that one of ordinary skill in the art would be apprised of what adaptations are necessary for a selected microbe. Thus the metes and bounds of the phrase are unclear. Therefore clarification is required to overcome the rejection.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
December 15, 2005

MARK NAVARRO
PRIMARY EXAMINER